

REMARKS

Status of the Claims

Claims 1-6 and 8-21 are pending. Claims 1, 2 and 12 have been amended, claim 7 has been cancelled and claims 20 and 21 have been newly added. Claims 10 and 13-19 are withdrawn from consideration.

No New Matter Has Been Added

Applicants submit that no new matter has been added by way of the present amendment. For instance, claim 1 has been amended to include subject matter taken from claim 7, now cancelled. Claim 2 has been amended to define the location of the chromophore as supported by the present specification at page 5, lines 19-21. Claim 12 has been amended to remove subject matter relating to preferred species. These preferred species have been added in new claim 20. Support for new claim 21 can be found in originally filed claim 7. Accordingly, no new matter has been added.

In view of the following remarks, Applicants respectfully request that the Examiner withdraw all rejections and allow the currently pending claims.

Election/Restriction

In the outstanding Office Action, the Examiner has reminded Applicants of the requirement to elect one of the following groups of claims:

- Group I: Claims 1-12, directed to proteins;
- Group II: Claims 13-18, directed to nucleotides; and
- Group III: Claim 19, directed to a method of use.

By telephone, Applicants' representative had previously elected Group I, with traverse. Applicants hereby affirm the election of Group I, with traverse. Applicants further submit that there is no undue burden placed on the Examiner to search and consider all of the claims in their entirety.

Additionally, the Examiner required election of a single amino acid sequence if Group I was elected. Applicants hereby affirm the election of SEQ ID NO.:4. However, Applicants submit that additional sequences should be searched. For instance, Applicants we note that the Examiner has not expanded the search to include other, non-elected species, for instance, SEQ ID NO:8 of claim 10. Rather, the Examiner has withdrawn this sequence from consideration.

Applicants submit that this is procedurally incorrect. Claim 1 represents a generic linking claim for both SEQ ID NO.4 and SEQ ID NO.8. Additionally, both SEQ ID NO.:4 and SEQ ID

NO.8 share common structural attributes, for instance, both sequences contain the position 64 and position 222 mutations, in particular, the F64L and E222G mutations. The difference between SEQ ID NO.: 4 and SEQ ID NO.:8 is their origin (what particular strain of jelly fish, still calling themselves *Aequoria Victoria*, were fished by the laboratory cloning it). Further, compared to SEQ ID NO: 8, SEQ ID NO: 4 is "enhanced" which includes, among other things, adding an amino acid in position 2 to provide a better cloning site and a Kozak sequence. Thus, in SEQ ID NO: 4 one should look for F65L and E223G, due to the additional upstream amino acid.

Accordingly, Applicants submit that claim 10 should be included within the Examiner's search and not withdrawn from consideration. Rejoinder of this claim is requested. Additionally, new claims 20 and 21 belong with Group I.

Issues Under 35 U.S.C. § 112, Second Paragraph

The Examiner has rejected claim 2 under 35 U.S.C. § 112, second paragraph, since the claim recites a range of "65-57" for the amino acid position of the chromophore. Applicants traverse and submit that this represents an inadvertent typographical error and should correctly read "65-67" as discussed at page 5, lines

19-21 of the present specification. Reconsideration and withdrawal of this rejection are requested.

Issues Under 35 U.S.C. § 103(a)

The Examiner has rejected claims 1-8 under 35 U.S.C. § 103(a) as being obvious over Thastrup et al., WO 97/11094 (hereinafter referred to as Thastrup) in view of Tsien et al., USP 6,124,128 (hereinafter referred to as Tsien). Applicants respectfully traverse this rejection.

The Examiner asserts that the Thastrup article discloses the F64L mutation of GFP and the Tsien reference discloses the E222G mutation of GFP. Applicants disagree with the Examiner's combination and reading of the cited art.

First, the Examiner indicates motivation exists to combine the references since the Thastrup references discloses that other mutations are possible preceeding the chromophore provided that they result in improved fluorescent properties of the various fluorescent proteins. However, Applicants point out that any mutation of the amino acid at position 222 would in fact proceed the chromophore in GFP. As noted above, the chromophore exists at positions 65-67 of GFP.

Second, even ignoring the lack of motivation, Applicants submit that the Examiner has misread the Tsien reference. The

Examiner asserts that Tsien discloses the E222G mutation, however, this is not the case. The Examiner refers to column 3, line 56 of Tsien as disclosing the E222G mutation. However, the referenced paragraph of Tsien specifically reads "not E222G".

In column 4, line 12 of Tsien, two mutations in position 222 are proposed: E222N and E222Q. Applicants direct the Examiner's attention to the fact that the present claims require any one of an E222G, E222A, E222V, E222L or E222I mutations, but not the E222N or E222Q mutations discussed by Tsien. Accordingly, even if one of ordinary skill in the art were motivated to combine the disclosure of Thastrup with Tsien, they would at most arrive at a F64L/E222N or F64L/E222Q protein, but not the currently claimed protein.

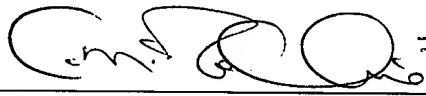
In summary, the Examiner has failed to present a valid *prima facie* case of obviousness. The disclosures of Thastrup and Tsien, whether taken alone or in combination, fail to suggest or disclose the presently claimed subject matter. Accordingly the Examiner is respectfully requested to withdraw all rejections and allow the currently pending claims.

If the Examiner has any questions or comments, please contact Craig A. McRobbie, Reg. No. 42,874, at the offices of Birch, Stewart, Kolasch & Birch, LLP.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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